REMARKS

Claims 1-59 are pending. Claims 1-25 and 45-53 are withdrawn according to the Restriction Requirement mailed October 2, 2008.

Claims 26, 27, 29-33, 34, 36-44 and 54-57 are currently amended for typographical reasons and clarity. Claims 58 and 59 are new. Support for the amendments to independent claim 26 and its dependent claims can be found in paragraphs 67 and 187 and throughout the specification as filed. Support for new claims 58 and 59 can be found in claim 26 and 31, paragraphs 45, 82, 95, 187 and throughout the specification as filed. Claims 26-44 and 54-57 stand rejected. No new matter is entered.

Reconsideration is respectfully requested in light of the following remarks.

Claim Rejections – 35 USC § 102(e)

Claims 26-38, 40, 42-44 and 54-57 are rejected under 35 U.S.C. 102(e) as being anticipated by US 2002/0194201 ("Wilbanks"). In the Office Action dated July 1, 2011 maintained in the Advisory Action, the Office asserts that the effective filing date under 35 U.S.C. 102(e) of Wilbanks is June 5, 2001 which is the earliest claimed priority via provisional application US 60/296,018. (See Office Action, page 10, par. 3).

Applicants respectfully traverse the basis that the subject matter relied upon by the Office Action is not entitled to the filing date of June 5, 2001 of US 60/296,018. In applying the discloseings of Wilbanks, the Office quotes exclusively from US Patent Publication 2002/0194201 (Wilbanks; Office Action dated July 1, 2011, pages 4-6). US 60/296,018, which the Office relies on to determine the effective filing date under 35 U.S.C. 102(e) of Wilbanks fails to disclose the discloseings of Wilbanks that the Office uses in claim rejections under 35 U.S.C. 102(e). For example, on pg. 4 last paragraph of the Office Action dated July 1, 2011, the Office alleges that "Wilbanks disclosees a query of results stored as at least one new relationship in the entity-relationship model and the establishment of a confidence level that is assigned to at least one of the relationships (paragraph 0013)". However, the provisional application US 60/296,018 is silent on any discloseing about the establishment of confidence levels. Thus, the filing date of US 60/296,018 is not available for the determination of the effective filing date under 102(e) of Wilbanks. The Office further argues in the Advisory Action (pg. 3 last par.) dated December 9, 2011 that US 60/356,616 filed February 13, 2002 is also relied upon as an effective filing date. The Office asserts that US 60/356,616 discloses "assign[ing] confidence levels and/or validity to relationships (page 5)". However, US 60/356,616 is silent about generating a **collection of profiles** according to **one or more profile generation criteria,** said profiles being suitable for "identify[ing] one

or more overlapped profiles from the collection of profiles that comprise an overlap with at least a portion of the user-supplied genomics data" and "determin[ing], for each of the one or more overlapped profiles, **whether the overlap is statistically significant**, wherein the determination permits all profiles to be compared in relative terms against each other as required by instant claim 26. The mere mention of assigning confidence levels to relationships in an ontology does not even suggest determining statistical significance **between a profile and at least a portion of user-supplied genomics data.** Thus, US 60/356,616 cannot be relied on for the effective filing date under 35 U.S.C. 102(e) of Wilbanks with respect to claim 26 of the instant application or any claims that depend from it. Applicants respectfully submit that the effective filing date under 35 U.S.C. 102(e) of Wilbanks is May 13, 2002, which is the actual filing date of the application published as US 2002/0194201.

Moreover, the invention as claimed in the instant Application was conceived and reduced to practice prior to May 13, 2002, as discussed below and as evidenced in the Declaration Under Rule 131 submitted previously. Therefore, for at least the reason that Wilbanks is not available as prior art under 35 U.S.C 102(e), the Applicant respectfully requests the claim rejections under 35 U.S.C. 102(e) be withdrawn.

However, to expedite prosecution, Applicants submit arguments below for Wilbanks failing to anticipate claims 26-38, 40, 42-44 and 54-57 even if it were available as prior art under 35 U.S.C. 102 (e). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Wilbanks fails to anticipate claims 26-38, 40, 42-44 and 54-57 because Wilbanks fails to disclose each and every element as set forth in the claims.

Claim 26:

Claim 26 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Applicants respectfully request the withdrawal of the rejection of claim 26 and its dependent claims for at least two reasons.

I. Wilbanks has no mention of generating profiles that are suitable for **identifying an overlap with at least a portion of a user-supplied genomics data** or determining statistical significance for such overlaps.

The Office asserts that paragraph 9 of Wilbanks disclosees the identification of related entities, thus discloseing overlapping information. Paragraph 9 of Wilbanks recites:

> Some embodiments of the present invention integrate a plurality of biological/chemical databases by obtaining an entity-relationship model for each of the plurality of biological/chemical databases, and identifying related entities, including identical entities, in the entity-relationship models of at least two of the biological/chemical

> databases. At least two of the related entities that are identified are linked, to thereby create an entity-relationship model that integrates the plurality of biological/chemical databases. In some embodiments, when the entities are identical entities, they are merged. In some embodiments, each of the plurality of databases represents an ontology and the entity-relationship model that integrates the plurality of biological/chemical databases creates an ontology network.

As seen in the above quote, the identification of related entities in Wilbanks is for assessing linkages between related and identical entities for the purpose of building a database. In contrast, claim 26 is drawn to a computer system that is configured to determine an overlap between a profile within the database and at least a portion of the user-supplied genomics information with statistical significance. Wilbanks has no mention of generating profiles that are suitable for identifying an overlap with at least a portion of a user-supplied genomics data or determining statistical significance for such overlaps.

II. Wilbanks does not disclose determining statistical significance for overlaps between a profile in a database and a portion of the user-supplied genomics data.

Wilbanks has several references to confidence levels all in the context of believability of relationships within their database. The Office cites paragraph 13 of Wilbanks for the establishment of a confidence level that is assigned to at least one of the relationships. Paragraph 13 recites:

> In other embodiments, the query results are stored as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases, to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases. In still other embodiments, a confidence level is assigned to at least one of the relationships in the entity-relationship model that integrates the plurality of biological/chemical databases. In still other embodiments, query results also may be based on assigned confidence levels.

Confidence levels are further described in paragraph 187 of Wilbanks as follows:

> Some relationships may be more certain than others. For example, an enzyme that is known to bind to a ligand is a high quality relationship. On the other hand, if a gene product is said to be related to a protein based on sequence homology of 30%, then that relationship may be of low quality. Therefore, in some embodiments, relationships may have a confidence value to reflect the quality of either the data source or the method used to specify that relationship. Confidence values allow a user to filter out relationships that are of too low quality for their purpose. Because of the confidence values, embodiments of the invention can also be thought of as a DWG.

As seen in the above quote, confidence levels of Wilbanks are a property of the data or relationships within an ontology. They are merely an indicator of quality for the information within the database. Claim 26 is drawn to a computer system that is configured to identify one or more overlapped profiles from the collection of profiles that comprise an overlap with at least a portion of the user-supplied genomics data and determine, for each of the one or more overlapped profiles, whether the overlap is

statistically significant. Wilbanks fails to disclose determining statistical significance for overlaps between a profile in a database and user-supplied genomics data.

The Office further cites paragraph 87 of Wilbanks for allegedly disclosinging cluster comparisons for data prediction and groupings. Paragraph 87 recites:

> Thus, some embodiments of the invention can provide a cross-reference query tool for searching across multiple databases, returning only entities which meet the specified query criteria in all databases. Other embodiments also can provide a translation and annotation tool that can allow translation from one naming system to another naming system, and automatic annotation of data files using different naming systems with description data from differing imported databases. Still other embodiments can provide a clustering engine and viewer, which can allow a user to take clustered experimental data from another program and compare it with data clustered by differing data types (e.g., molecular function) to see how well the experimental clusters predict the annotation clusters and if there are additional annotation clusters. Finally, still other embodiments can provide an unsupervised grouping search, which can take a list of clustered biological entities (e.g., genes showing a similar expression pattern) and can automatically generate a hypothesis of why they are grouped.

This paragraph, as well, fails to disclose an overlap between user-supplied genomics data and one or more profiles in a database that is **statistically significant**. A user is left to take "experimental data from another program and compare it with data clustered by differing data types", however, no disclosure is provided for determining the statistical significance of this comparison. Thus, Wilbanks fails to anticipate independent claim 26.

Claim 27:

Claim 27 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 27 depends from claim 26 and is drawn to a computer system with a computer that is "configured to pre-generate a profile library containing a profile for each one of a genomic information type in the structured database according to the profile model."

The Office cites paragraph 69 of Wilbanks for allegedly disclosing a priori data built in to the system. Paragraph 69 recites:

> Referring now to FIG. 3, a data processing engine 300, which also may be referred to as an ontology engine, can be used to integrate, update and/or query a plurality of databases, and/or generate, add to and/or query an ontology network as will be described in detail below. The engine 300 can provide a knowledge mining layer 110 of FIG. 1 and/or an ontology network 210 of FIG. 2 in some embodiments. The engine 300 is responsive to one or more loaders 302 that can extract relevant information from one or more biological/chemical databases 304, which can be analogous to the data collection layer 104 of FIG. 1 and/or the databases 202, 208 of FIG. 2. In some embodiments, a priori knowledge of the semantics of the ontology that is represented by the associated biological/chemical databases 304 is built into the loader 302 of that ontology's external data files. Moreover, in some embodiments, the loader 302 has knowledge of the semantics of the appropriate part of the engine 300, to which the ontology data connects.

This cited paragraph merely discloses a generalization of a database, not a profile library as required by claim 27. Thus, Wilbanks fails to anticipate claim 27.

Claim 28:

Claim 28 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 28 depends from claim 27 and is drawn to a computer system with profiles that are pre-generated from a graph structure.

The Office cites paragraph 86 of Wilbanks for allegedly disclosing profiles generated from graph structures and refers to DWG. Paragraph 86 recites:

> Additional qualitative discussion of integration and/or querying of biological/chemical databases according to some embodiments of the present invention that were described in FIGS. 5-7 now will be provided. In particular, some embodiments of the invention can import different types of experimental, sequence, chemical, annotation, or other data from a Tab-Separated-Value (TSV) format, a simple eXtensible Markup Language (XML) format and/or other formats. Scripts may be provided to convert all common data formats to this TSV, XML and/or other formats. Some embodiments can create biological entities with many different aliases, parents and children. Entities can be merged if they are found to be equivalent. The entities may be organized in Directed Weighted Graph (DWG) based ontologies, as well as hierarchical and/or single level classifications. For non-expert users, a HyperText Markup Language (HTML)-based database viewer, which allows the user to search for terms and then move between different entities via hyperlinks, may be provided. Other embodiments also can produce a tool for traversing across multiple relationships to construct a logical path. Yet other embodiments can provide a tool for importing stored traversals in order to automatically execute those traversals across multiple entities.

This reference merely discloses the structure of the Wilbanks ontology and how entries within it can be organized. There is, in fact, no disclosure in Wilbanks about pre-generating **profiles** from graph structures as in the instant claim.

Claim 29:

Claim 29 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. As amended claim 29 depends from claim 26 and is drawn to a computer system with a computer that "is further configured to generate the profiles by querying the structured database for information matching the one or more profile definition criteria".

The Office cites paragraph 13 of Wilbanks and asserts that it discloses data query. Paragraph 13 recites:

> In other embodiments, the query results are stored as at least one new relationship in the entity-relationship model that integrates the plurality of biological/chemical databases, to thereby store knowledge that was derived from the query in the entity-relationship model that integrates the plurality of biological/chemical databases. In still other embodiments, a confidence level is assigned to at least one of the relationships in the entity-relationship model that integrates the plurality of biological/chemical databases. In still other embodiments, query results also may be based on assigned confidence levels.

Paragraph 13 has no description of generating profiles or the one or more profile criterion. In fact, Wilbanks does not disclose generating profiles according to a profile definition criterion as required by claim 26. Wilbanks merely discloses ways to *discover* new relationships between entities in the database by exploring whether a path exists between the two entities (see e.g. par. 162). Not only does Wilbanks fail to disclose a system that is configured to generate profiles that are suitable for identifying an overlap with at least a portion of a user-supplied genomics data, by querying the database as required by claim 29, there is in fact no disclosure in Wilbanks for generating profiles according to profile generation criteria as required by claim 26. Thus, Wilbanks fails to anticipate claim 29.

Claim 30:

Claim 30 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 30 depends from claim 28 and is drawn to "the computation of a probability of overlap as a function of information contained in the structured database" for "the determination of whether the overlap is statistical significant".

The Office cites paragraphs 84, 132, and 133 of Wilbanks for disclosing probability calculations/likelihood of success predictions. Paragraph 84 refers to "extracting traversal patterns related to likelihood of success" based on stored data related to successful drug discoveries:

> In yet other embodiments of the invention, when the data structure is updated by addition, deletion and/or splitting, an image, instance or version of the earlier data structure may be maintained. This image may be used for archival purposes, to ascertain the state of the data structure during a discovery, according to some embodiments of the invention. In other embodiments, comparisons may be made between different images of the data structure, to itself lead to new discovery. Thus, for example, one image of the entity-relationship model can store data related to successful drug discoveries, from genomic to clinical indicators, to extract traversal patterns related to likelihood of success. Another image can store a similar set of patterns for expensive drug failures that did not make it through a genomic, pre-clinical or clinical phase. These images can be compared in order to obtain discovery that can predict success.

To reiterate, there is no disclosure of statistical significance considerations for the overlap between user-supplied data and one or more profiles as required by the claim. The use of the "likehood of success" in this context has no relationship to a statistical likelihood calculation and is merely used in a

colloquial way for qualitatively, but not quantitatively or statistically extracting a pattern. There is no description of how a probability of overlap and a statistical significance can be determined. In contrast, claim 30 requires the computation of a probability of overlap as a function of information contained in the structured database" for "the determination of whether the overlap is statistical significant.

Paragraph of Wilbanks 132 recites:

> According to some embodiments of the invention, an ontology network 210 can reside as a part of an information stack related to the basic scientific experiments where enormous quantities of data are collected, for example as was shown in FIG. 2. In some embodiments, the ontology network can be located above a conventional integration tool or layer 206 and can provide a knowledge mining tool or layer 110 that can be available for hypothesis or question-driven mining as opposed to complex data mining queries typical of data mining applications. Some embodiments of the ontology network can comprise a meta database of terms, entities and/or data relationships that can provide for a more efficient and intelligent analysis of accumulated data.

Paragraph of Wilbanks 133 recites:

> According to other embodiments of the invention, implementation of virtual experiments 112 and discovery 212 that employ this ontology network can provide inference engines. As is well known, the components of an expert system are a knowledge base, which may be implemented according to embodiments of the invention by an ontology network 210, and an inference engine which performs reasoning. According to some embodiments, an inference engine or reasoning software application searches and creates rules by determined pattern matching and then establishes new rules and develops forward chaining of rules. Virtual experiments 112 within the subject field of inquiry can be executed which can significantly enhance accuracies and/or have abilities to correlate observations to original predictive behavior with a broader input of related information than previously may be employed.

Paragraphs 132 and 133 also fail to disclose the determination of statistical significance between user-supplied genomics data and one or more profiles. These paragraphs are drawn to exploring the database for finding previously unidentified relationships between entities in the database. The mere mention of a term related to probability calculations does not anticipate a specific determination of statistical significance between user-supplied genomics data and one or more profiles and certainly does not disclose the determination of statistical significance between the two "as a function of information contained in the database" as required by claim 30. Applicants submit that claim 31 is not anticipated by Wilbanks.

Claim 32:

Claim 32 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 32 depends from claim 26 and is drawn to the user-supplied genomics data comprising differential gene expression data.

The Office cites paragraph 87 of Wilbanks for allegedly disclosing differential gene expression data. Paragraph 87 recites:

> Thus, some embodiments of the invention can provide a cross-reference query tool for searching across multiple databases, returning only entities which meet the specified query criteria in all databases. Other embodiments also can provide a translation and annotation tool that can allow translation from one naming system to another naming system, and automatic annotation of data files using different naming systems with description data from differing imported databases. Still other embodiments can provide a clustering engine and viewer, which can allow a user to take clustered experimental data from another program and compare it with data clustered by differing data types (e.g., molecular function) to see how well the experimental clusters predict the annotation clusters and if there are additional annotation clusters. Finally, still other embodiments can provide an unsupervised grouping search, which can take a list of clustered biological entities (e.g., genes showing a similar expression pattern) and can automatically generate a hypothesis of why they are grouped.

However, paragraph 87 makes no mention of **differential** gene expression data, but merely mentions expression patterns. Wilbanks generally fails to disclose differential gene expression data and thus fails to anticipate the limitations of the dependent claim 32.

Claim 33:

Claim 33 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 33 depends from claim 32 and is drawn to the user-supplied differential gene expression data relating to a particular disease.

The Office cites paragraph 112 of Wilbanks for allegedly disclosing disease data:

> Using some embodiments of the invention: The user can use a relationship finder tool and enter the CSR2_RAT and Leukemia. Some embodiments of the invention can perform a breadth-first search, traversing any kind of relationship and can tell the user that "CSR2_RAT shares Pfam: LIM with RHM1_HUMAN. RHM1_HUMAN is related to OMIM-DISEASE: Leukemia".

Paragraph 112 mentions leukemia as a disease, however there is no disclosure of differential gene expression data that relates to leukemia or any other disease in this paragraph or elsewhere in Wilbanks as required by the limitation of dependent claim 33. Thus, Wilbanks fails to anticipate claim 33.

Claim 34:

Claim 34 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 34 depends from claim 26 and is drawn to "the one or more profile generation criteria compris[ing] one or more of a biological process, number of genes, organismal process, gene connectivity, edge connectivity, findings source type, experiment context, or tissue consistency criterion."

The Office cites paragraph 135 of Wilbanks for allegedly disclosing profile generation criteria using biological processes. Paragraph 135 recites:

> As was described above, according to some embodiments of the present invention, an ontology network is created by merging, overlaying and/or linking identical objects and/or establishing a relationship between objects/entities in different ontologies. FIGS. 12-17 conceptually illustrate an example of the creation of an ontology network according to some embodiments of the present invention.

However, paragraph 135 and Wilbanks in general merely describe methods to generate an ontology but not profiles. Therefore, there is no disclosure of profile generation criteria, which comprise a biological process, number of genes, organismal process, gene connectivity, edge connectivity, findings source type, experiment context, or tissue consistency criterion and which can be used to generate profiles that are suitable for identifying an overlap with at least a portion of a user-supplied genomics data, either, as required by dependent claim 34.

Claim 35:

Claim 35 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 35 depends from claim 26 and is drawn to the profiles being "generated from a seed node" and "the inspection of database-asserted biological interactions focus[ing] on the biological interactions emanating from the seed node".

The Office cites paragraph 89 of Wilbanks for allegedly disclosing profile generation from nodes. Paragraph 89 recites:

> Some embodiments of the invention can generate, expand, update and/or query a data structure containing many nodes, each representing a biological entity (such as a protein, a gene, a protein family, or a literature reference) with multiple aliases. Using biological entity nodes, rather than a different table for each database (as in a star schema), means that all records in diverse biological/chemical databases that represent the same object can be merged into a single entity. For example, many "integrated" databases, include a table of SWISS-PROT records and a table of PIR records, which would be joined by a reference point or hub. A cross-reference in the SWISS-PROT entry may indicate that it is the same protein as a PIR entry. In contrast, in some embodiments of the invention, these records are used to create a single biological entity, label it with a category "protein" and establish aliases from both SWISS-PROT and PIR so it can be referenced using either naming system.

However, Applicants submit that the above cited paragraph fails to disclose profile generation from a seed node as required by claim 35. First, there is no disclosure of a "seed node" that serves for the "inspection of database-asserted biological interactions focusing on the biological interactions emanating from the seed node", as required by claim 35. Second, the nodes are mentioned in the context of building and querying a data structure with biological entities with multiple aliases. Thus, the nodes are used at best to merge data from multiple databases and relate relevant information with each other. The nodes merely serve to relate information from multiple data sources in a single data structure. However, there is no disclosure of generating profiles from these node structures.

Claim 36:

Claim 36 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 36 depends from claim 35 and is drawn to the seed being selected from the group of genomic data types consisting of a gene, gene product, and biological process.

The Office is citing paragraph 89 of Wilbanks again for allegedly disclosing nodes that are genes proteins, gene families etc. Claim 36 depends from claim 35 and thus par. 89 fails to anticipate the claim limitations of claim 36 for at least the reasons cited for claim 35.

Claim 37:

Claim 37 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 37 depends from claim 26 and is drawn to a computer system with a computer that is "further configured to compute a statistical significance for a biological association in the one or more overlapped profiles that are determined to comprise a statistically significant overlap".

The Office asserts that paragraphs 18, 52, 65, 84, and 87 of Wilbanks disclose comparisons to generate biological associations of the different profiles. Applicants believe that the Office misconstrues claim 37. Claim 37 is drawn to a computer that is configured to compute a statistical significance for a biological association, the biological association being within the one or more statistically significant profiles. First, Wilbanks does not disclose the determination of statistical significance for the one or more profiles that overlap with the user-supplied genomics as required by claim 26 and discussed above. As claim 37 requires for a biological association within a statistically significant profile, Wilbanks also fails to disclose the biological association, let alone computing a statistical significance for the biological association, as Wilbanks fails to disclose generating profiles that are suitable for identifying an overlap with at least a portion of a user-supplied genomics data or determining statistical significance for such overlaps..

Claim 38:

Claim 38 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks. Claim 38 depends from claim 27 and is drawn to "the pregeneration of a profile library compris[ing] the selection of a node for a profile based on a number of similar findings in the structured database that link the node to a neighboring node".

The Office cites paragraph 65 of Wilbanks and argues that it discloses the claimed data linkages. Paragraph 65 recites:

> As will be described in more detail below, according to some embodiments of the present invention, an ontology network 210 can incorporate the entity-relationship models of the databases on which it is built, but can also define new relationships or hierarchies by the process of overlay, merge and/or association of entities from the independent ontologies. This conceptualization of knowledge can serve as a specification mechanism for the development of a broad-mesh belief system that can deliver experimental insight. Stated differently, ontology networks 210 according to some embodiments of the present invention can traverse and, thereby, establish a linked path of relationships creating associations between characteristically unlike entities, to thereby allow the revelation of new information and knowledge. The resulting lattice of semantically rich metadata can form an ontology network 210 that captures the knowledge from the data sources 202, 208 it supports.

Accordingly, paragraph 65 of Wilbanks discloses discovery and incorporation of entities in an ontology network that are linked. In contrast, claim 38 firstly refers to nodes that are linked within **a profile** that is built according to a profile model using genomics information stored in the database, as opposed to nodes that are linked broadly within an entire ontology network as described in paragraph 65. Further, claim 38 requires not only a count of similar findings linking a node to a neighboring node, it further requires the selection of the node to be based on this count. Paragraph 65 fails to disclose nodes within a profile as well as their finding-count-based selection and therefore fails to anticipate the limitations of claim 38.

Claim 40, 42:

Claim 40 and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks.

Claim 40 depends from claim 26 with the additional limitation that the computer is "configured to annotate the profiles with biological associations asserted by the structured database wherein the associations comprise one or more of a cellular process, molecular process, organismal process or disease process". Claim 42 further adds the limitation that "the annotation of profiles comprises use of classification information found in an ontology". As discussed previously, Wilbanks does not disclose profiles that are suitable for identifying an overlap with at least a portion of a user-supplied genomics data or determining statistical significance for such overlaps. As a corollary, Wilbanks fails to disclose the

annotation limitations regarding the profiles of claim 26. Therefore, Wilbanks fails to anticipate claims 40 and 42.

Claim 44:

Claim 44 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks.

Claim 44 requires that the pre-generation of a profile library in claim 27 includes generating a plurality of profile libraries, each profile library corresponding to a different profile generation criterion The Office cites paragraphs 69 and 130 of Wilbanks for allegedly disclosing profile models using different criteria. However, both paragraphs 69 and 130, as well as Wilbanks as a whole refer to methods of generating an ontology and not profiles within it, and certainly not multiple profile libraries. For example, paragraph 69 recites:

> Referring now to FIG. 3, a data processing engine 300, which also may be referred to as an ontology engine, can be used to integrate, update and/or query a plurality of databases, and/or generate, add to and/or query an ontology network as will be described in detail below. The engine 300 can provide a knowledge mining layer 110 of FIG. 1 and/or an ontology network 210 of FIG. 2 in some embodiments. The engine 300 is responsive to one or more loaders 302 that can extract relevant information from one or more biological/chemical databases 304, which can be analogous to the data collection layer 104 of FIG. 1 and/or the databases 202, 208 of FIG. 2. In some embodiments, a priori knowledge of the semantics of the ontology that is represented by the associated biological/chemical databases 304 is built into the loader 302 of that ontology's external data files. Moreover, in some embodiments, the loader 302 has knowledge of the semantics of the appropriate part of the engine 300, to which the ontology data connects.

Paragraph 130 recites:

> Additional qualitative discussion of creation of an ontology network according to some embodiments of the present invention now will be provided. Some embodiments of the invention can overlay/merge/associate ontologies and provide extensive cross referencing to other existing data bases, data tables, data repositories, and ontologies. According to some embodiments of the invention, the resulting knowledge layer can provide an ontology network where multiple ontologies and various entities have been linked. The ontology network can bridge previously disparate data repositories, bringing structure to a previously amorphous assembly of independent ontologies of entities and relationships.

The cited paragraphs further fail to disclose multiple profile generation criteria as required by claim 44. Rather, the paragraphs relate to building a large ontology network from existing databases and provide solutions, such as loading a priori knowledge of the semantics of the ontology into a loader. Thus, claim 44 is not anticipated by Wilbanks.

Claim 54:

Claim 54 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks.

Claim 54 depends from claim 33 with differential gene expression data, with the computer being "further configured to analyze the user-supplied genomics data to identify a new use for a known therapy wherein the differential gene expression data relates to a pathway affected by the known therapy".

The Office cites paragraph 112 of Wilbanks for allegedly disclosing gene associations for disease. However, paragraph 112 merely discloses a relationship finder tool that is able to return associations of certain proteins with disease:

> Using some embodiments of the invention: The user can use a relationship finder tool and enter the CSR2_RAT and Leukemia. Some embodiments of the invention can perform a breadth-first search, traversing any kind of relationship and can tell the user that "CSR2_RAT shares Pfam: LIM with RHM1_HUMAN. RHM1_HUMAN is related to OMIM-DISEASE: Leukemia.

On the other hand, paragraph 112 fails to disclose the limitations of claim 54. As amended claim 54 requires a known therapy and a pathway affected by said therapy related to the differential gene expression data. The claim is drawn to a computer system with a computer that is configured to analyze the user-supplied genomics data to identify a new use for said known therapy. Paragraph 112 does not even mention the use of known therapies, let alone gene expression data related to a pathway that is affected by the known therapy. Further, there is no mention of finding a new use for a therapy. For at least these reasons, paragraph 112 fails to anticipate claim 54.

Claim 55:

Claim 55 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks.

Claim 55 depends from claim 33 with user-supplied gene expression data, with the computer being "further configured to analyze the user-supplied genomics data prioritizing candidate development compounds for further development by giving higher priority to development compounds on the basis of whether or not they are likely to result in an undesirable effect based on their involvement in other biological pathways as embodied in one of the one or more overlapped profiles".

The Office cites paragraph 120 of Wilbanks for allegedly disclosing candidate development compounds:

> It also will be understood that although embodiments of the invention have been described above with respect to genes, proteins, literature references, domains, ontologies and other data types, the ways in which data can be categorized and cross-referenced using embodiments of the invention can be virtually unlimited. For example, the description lines of genes from Hugo may be used in order to group them into sets of mutant alleles. A combination of Medline and expression data may be used to infer

> groupings on the basis of likely interactions. Also, high-throughput screening data may be used to cross-reference chemicals to genes and then group the chemicals by structure. Many other databases also can be used.

Paragraph 120 describes cross-referencing chemicals to genes. In contrast, claim 55 requires prioritizing development compounds on the basis of likelihood to result in an undesirable effect based on their involvement in other biological pathways as embodied in a profile. Paragraph 120 makes no mention of cross-examining the effects of a compound on its involvement with more than one biological pathway within a profile. In fact, there is no disclosure in Wilbanks of profiles as required by claim 26 and compounds within the context of profiles. In addition, paragraph 120 does not disclose prioritizing any compounds and certainly not for further development. Thus, Wilbanks fails to disclose the limitations of claim 55.

Claim 56:

Claim 56 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks.

Claim 56 depends from claim 33 adding the limitation requiring the computer to be "further configured to analyze the user-supplied genomics data to identify disease-related pathways wherein the disease is a side effect of drug therapy".

The Office cites paragraphs 112 and 120 of Wilbanks for allegedly disclosing disease-related pathways. However, these paragraphs make no mention of analyzing user-supplied genomics data comprising differential gene expression, identifying disease related-pathways, or a disease that is the side effect of drug therapy, all which are required by claim 56. Thus the reference fails to anticipate claim 56.

Claim 57:

Claim 57 is rejected under 35 U.S.C. 102(e) as being anticipated by Wilbanks.

Claim 57 depends from claim 33 with the additional limitation requiring the differential gene expression data to relate "to a particular disease" and "analysis of one or more statistically significant overlapped profiles together with the user-supplied genomics data further comprises validating whether the differential gene expression data comprise genotypic markers for the disease according to whether a database-asserted biological association related to the disease, which is shared among a plurality of overlapped profiles, is statistically significant".

The Office cites paragraphs 120, 193-195 of Wilbanks for allegedly disclosing gene expression linked to markers which are linked to disease states. First, the paragraphs describe tissue specific gene expression of a gene that is linked to asthma. However, the reference fails to disclose a link between its expression and the disease. In contrast, claim 57 treats as a set of markers. The validation as markers for a

particular disease is achieved by determination of a statistically significant biological association related to the disease shared among a plurality of profiles. As previously discussed, Wilbanks does not disclose statistically significant determination of overlapping profiles as required by the related independent claim 26, let alone "a database-asserted biological association related to the disease state" being "**shared** among a **pluraility of overlapped profiles**" or the **statistical significance** of said shared biological association. A shared biological association among multiple profiles is simply not described. For these at least these reasons claim 57 is not anticipated by the reference.

Claim Rejections – 35 USC § 103(a)

Wilbanks is not available as prior art:

The claim rejections under 35 U.S.C. 103(a) rely on Wilbanks as the primary reference. As discussed above, the subject matter relied upon in the rejection is not present in US 60/296,018. Thus, the effective filing date of Wilbanks is after the conception and reduction to practice of the instant claims as evidenced in the Declaration Under Rule 131 submitted previously. As Wilbanks is not available as prior art, and neither Karp nor Qu separately or combined render the instant claims unpatentable, Applicants respectfully request that the claim rejections under U.S.C. 35 103(a) be withdrawn.

However, to expedite prosecution, Applicants submit arguments below rebutting the 35 U.S.C. 103(a) rejections for claims 39, 41 and 43, even if Wilbanks were available as prior art under 35 U.S.C. 102(e).

Claims 39 and 41:

Claims 39 and 41 are rejected under 35 U.S.C. 103(a) as allegedly being obvious over US 2002/0194201 (Wilbanks), as applied to claims 26 and 40, and further view of Karp et al. (TIBTECH (1999) Vol. 17, pages 275-281; IDS reference; herein Karp). Claim 39 depends from claim 26 and in addition to all of the limitations of claim 26 includes the limitation that the "computer is further configured to display information related to the one or more overlapped profiles that are determined to comprise a statistically significant overlap and the user-supplied genomics data using a GUI". Claim 41 depends from claim 40 and in addition to all of the limitations of claim 40, requires that the "computer is further configured to display biological associations using one of a GUI or a report". The Office relies on Wilbanks as meeting the claimed elements of independent claim 26 and dependent claim 40, and combines the discloseings of Wilbanks with Karp to arrive at the claimed elements of claims 39 and 41.

Applicants respectfully traverse, as the combination of Wilbanks and Karp fail to disclose all of the limitations of claim 39 and 41.

As discussed above with respect to the rejection of claims 26 and 40 under 35 U.S.C. 102(e), Wilbanks fails to describe generation of profiles that are suitable for identifying an overlap with at least a portion of a user-supplied genomics data or determining statistical significance for such overlaps, determination of statistical significance for overlaps between a profile in a database and a portion of the user-supplied genomics data, or annotation of the profiles with biological associations asserted by the structured. Karp fails to remedy the deficiencies of Wilbanks with respect to these required elements of claim 26 and 40. Karp also fails to disclose profiles that overlap with user-supplied genomics data with statistical significance.

Applicants respectfully request withdrawal of the rejection.

Claim 43:

Claim 43 is rejected under 35 U.S.C. 103(a) as allegedly being obvious over US 2002/0194201 (Wilbanks), as applied to claim 26, and further view of Qu et al. (Intelligent Systems in Biology (2002) March/April, pages 21-27; IDS reference; previously cited; herein Qu). The Office Action relies on Wilbanks as meeting the claimed elements of independent claim 26, and combines the discloseings of Wilbanks with Qu to arrive at the claimed elements of claims 43. Applicants respectfully traverse.

As discussed above with respect to the rejection of claims 26 and 40 under 35 U.S.C. 102(e), Wilbanks fails to describe profiles that overlap with user-supplied genomics data with statistical significance. Qu fails to remedy the deficiencies of Wilbanks with respect to these required elements of claim 26. Thus, the combination of Wilbanks and Qu fail to disclose all of the limitations of claim 26. Since claim 43 depends from 26 and incorporates all of the limitations of claim 26, the combination of Wilbanks and Qu also fail to disclose all of the limitations of claim 43.

Qu also fails to teach or suggest "a test of a null hypothesis over a discrete probability distribution, the distribution being a function of database size, profile sizes, the user-supplied genomics data size and expression values". The Office alleges that Qu discloseses "the calculation of relationship inference by statistical methods such as cluster analysis using hirrarchical clustering employing the Pearson correlation coefficient to construct a relationship tree (page 24, column 3)". However, "[h]ierarchical clustering offers statistical assessment of members' relatedness along a **branching tree**" (page 24, column 3). Thus, the hierarchical clustering has nothing to do with overlapping profiles with user-supplied genomics data. Furthermore, no test of null hypothesis is described in Qu. In addition, a probability distribution that is a function of database size, profile sizes, the user-supplied genomics data size and expression values is not described in Qu. Thus, Wilbanks and Qu, either alone or in combination,

not only fail to teach or suggest each and every limitation of the independent claim 26, they also fail to teach or suggest all of the limitations of claim 43.

Further, one of ordinary skill in the art at the time of the invention would not have used a probability distribution "being a function of database size, profile sizes, the user-supplied genomics data size and expression values" as required in claim 43. First, many of the variables of the probability function of claim 43 are not recognizedas variables in Wilbanks or Qu. Therefore, based on the teachings of the cited art, one skilled in the art would not know to construct a probability function with these variables as they are not taught in Wilbanks or Qu. As such, it would not have been prima facie obvious for one of ordinary skill in the art to construct a probability function including the variables required in claim 43 based on the teachings of Wilbanks and Qu. Second, the probability distribution of claim 43 is a specific function and one skilled in the art would not know to select this function among the many possibilities without undue experimentation, even if some or all of the required variables were taught by Wilbanks or Qu.

Applicants respectfully request withdrawal of the rejection.

Declaration Under 37 CFR 1.131

In the Office Action dated July 1, 2011, the Examiner states that "[t]he Declarations filed on 7 March 2011 under 37 CFR 1.131 have been considered but are ineffective to overcome the prior art reference"(see Office Action dated July 1, 2011, pg. 10, par. 1, and further Advisory Action dated December 9, 2011, pg. 4 par. 1-2). Applicants respectfully traverse based on the arguments included in their December 1, 2011 Response to the Final Office Action dated July 1, 2011.

Applicants are entitled to the claimed February 4th 2002 priority date based upon US 60/353,176

The Office denied the priority claim to US 60/353,176, arguing that the provisional application does not disclose profile models and the building of profiles according to genomics information that is identified for overlap and statistically analyzed to establish biological interactions.

In fact, on page 10, the 3rd complete paragraph of US 60/353,176 states in part that "it is practical to query the knowledge representation system for concepts, e.g. genes and gene products, related to a disease and thereby to construct a disease-related pathway that extends back several steps, and that branches out to identify overlapping disease-related pathways". Further, steps of a method for identifying a candidate drug discovery target are listed in part on page 11 of US 60/353,176 and step (b)_includes "querying the database to identify a disease-related pathway." At the same time, the storage means in step

(a) "permits computational analysis of complex relationships among the stored concepts". The last paragraph on page 12 of US 60/353,176 states means to "identify all pathways in which the target of the known drug is involved, additional to the pathway for the disease for which the drug is indicated." Thus, US 60/353,176 describes methods and means to define sub-sets within a knowledge representation system for concepts, e.g. genes and gene products, related to a disease, according to desired criteria, i.e. a profile model based on one or more profile definition criterion, as required by claim 26.

Further, on pages 3-4 of US 60/353,176 the Summary of the Invention states in part that "the invention relates to methods of identifying drug discovery targets by defining disease pathways by computer analysis of direct as well as complex relations among different genes or gene products." On page 4 of the specification it states "[t]he invention makes use of structured database representation of information concerning genes, gene products and phenotypic traits of interest, and optionally other information such that relationships that are several steps removed and may be multidirectional, can be identified." On page 5 it is stated that "in a preferred embodiment, information is stored in, and accessed using an ontology," "the domain of interest is genomic information," and "an ontology stores its contents in a frame-based format that allows searching of the ontology to find relationships between or to make inferences about items stored in the ontology." Page 7 describes "fact templates" which are placed in the ontology. Page 8 describes types and gives examples of genomics information that can be translated into the ontology. Finally, claim 1 of US 60/353,176 includes "computational analysis of complex relationships among the stored concepts."

Accordingly, US 60/353,176 discloses profile models and the building of profiles according to genomics information that is identified for overlap and statistically analyzed to establish biological interactions. Thus the correct priority date for the instant application should be February 4th 2002 based upon US 60/353,176.

CONCLUSION

In light of the remarks set forth above, Applicants believe that they are entitled allowance of the applicaion. Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner have any question, the Examiner is encouraged to telephone the undersigned.

The Commissioner is authorized to charge any underpayment or credit any overpayment to Deposit account No. 23-2415 (Attorney Docket No. 27763-705.831) for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

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